REMARKS

A. The Status of the Claims and the Amendments

Claims 105-120 are pending. Claims 106 and 107 have been withdrawn from consideration as claims directed to non-elected matter. The Applicants acknowledge the fact that the restriction requirement has been made final.

By the present amendment, claims 105, 117, 119, and 120 have been amended to more particularly define the Applicant's invention and to claim it with greater specificity. Claims amendments are supported by the specification and the original claims. No new matter have been added.

It is submitted that the amendments place the claims in condition for allowance. Entry of the amendments is respectfully requested. After the amendments have been entered, claims 105 and 108-120 will be under examination.

B. Rejection Under 35 U.S.C. § 112, First Paragraph (Written Description)

Claims 119 and 120 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement (page 3, lines 13-14 of the Office Action), due to alleged introduction of new matter. The Examiner has stated that the limitation "200-500 milliwatts per cm^2" constitutes a new matter. This rejection is respectfully traversed on the ground that the Examiner is mistaken and there is no new matter.

Indeed, it is respectfully submitted that the specification as filed discloses a typical range of energies being applied as "from about 200 milliwatts per cm^2 to about 10 watts per cm^2" (see, lines 7-8 of paragraph [0121] on page 18 of the published application US2005/0080029). Clearly, the upper limit of the range recited in claim 119 (i.e., 500 milliwatts per cm^2 which is the same as 0.5 watt per cm^2) is above the lower limit recited in the original specification (i.e., 200 milliwatts per cm^2) but below the upper limit recited in the original specification (i.e., 10

watts per cm^2). Thus, the range recited in the instant claim 119 is completely within the range recited in the original specification. It is, therefore, elementary, that the matter recited in claim 119 is disclosed in the original specification.

Accordingly, the Applicants respectfully submit that the written description requirement has been satisfied with respect to claims 119-120, and that there is no new matter. Reconsideration and withdrawal of the rejection are respectfully requested.

C. Rejections Under 35 U.S.C. § 112, First Paragraph (Enablement)

Claims 105 and 108-120 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which allegedly was not described in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention (page 5, lines 4-11 of the Office Action). This rejection is respectfully traversed on the ground that the Examiner has not met the burden of demonstrating that the entire breadth and scope of the claims is allegedly not enabled.

The burden of demonstrating that the claims are not properly enabled is n the Examiner, as required by In re Wright, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). It has been established that a presumption of enablement exists, and that ordinarily the lack of enablement rejection should not be given unless there are reasons to doubt the veracity of the statements in the application upon which the reliance for enablement is based. MPEP § 2164.04. It is respectfully submitted that in this case the Examiner has not met the burden of demonstrating the alleged lack of enablement.

The legal standard for determining the adequacy of enablement is clear. To be enabling, "the specification of the patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation." Genentech Inc. v. NovoNordisk, 108 F.3d 1361, 42 USPQ2d 1001 (Fed. Cir. 1997). The Applicant submits that the specification does comply with the enablement requirement.

The Examiner has stated that the enablement requirement has not been satisfied because the specification does not provide enablement other than for a method that utilizes a nucleic acid as a compound to be delivered (see, page 5, lines 5-11). The Examiner has further asserted that practicing the invention as now claimed will require undue experimentation (see, page 6, lines 13-16), and names, among other reasons, the fact that the variety of compounds to be delivered, as claimed, makes claims of "essentially unlimited scope" (see, page 6, lines 13-16). The Applicants respectfully disagree and submit that the specification provides enough details on how to practice the method.

Claims 105 and 119 have been amended, reciting not just any compound to be delivered, but a "therapeutically beneficial compound," thus narrowing the claims to a more reasonable breadth. While the specification does not expressly provide actual examples directed to delivering compounds other than nucleic acid sequences, one skilled in the art would clearly understand that the technique and methodology that is provided for delivery nucleic acid sequences would equally apply to delivering other pharmaceutical agents.

The Applicants further point out that it is well known in the art that the delivery of many materials to a cell is often very difficult, particularly if the materials to be delivered have low aqueous solubility. One solution of this problem is proposed in the instant application, i.e., improvement of delivery using organic halides in combination with the application of ultrasound. Thus, it is combining the therapeutically beneficial compound with a halide and applying ultrasound that lead to improved transfection. The Applicants respectfully represent that once this technique is taught with respect to one therapeutically beneficial compound (i.e., a nucleic acid sequence), those skilled in the art would necessarily understand that the same general methodology can be easily utilized with respect to other therapeutically beneficial compound(s).

The case law is clear that as long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement is satisfied. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The Examiner has conceded that the claimed method is enabled

when the compounds to be delivered is a nucleic acid sequence. The entire scope of claims in the instant application includes steps for delivering a therapeutically beneficial compound.

Examples provided in the specification teach how to practice the method, and specify, for nucleic acid sequences, each step of the process, including mixing with a halide, and applying ultrasound. The specification teaches every step of the method by providing every relevant detail of the process. Based on what is exemplified in the application, all that a person having ordinary skill in the art would need to practice the invention with respect to other therapeutically beneficial compound(s), would be to make a halide-containing composition, where a nucleic acid sequence is replaced with such other therapeutically beneficial compound. In addition, because the composition would not contain a nucleic acid sequence, but would rather include another therapeutically beneficial compound, adjustments may need to be made with respect to the ratios of the compounds in the composition and with respect to the protocol of applying ultrasound. It is respectfully submitted that making such adjustments is not a complicated process, and is well within capacities of those skilled in the art, particularly in view of the guidelines provides in the application. No undue experimentation would be needed to arrive at optimal conditions.

Referring to the case law discussed above, it is submitted that Fisher does not require a complete correspondence between the disclosure and the scope of a claim. What Fisher does require is only a **reasonable, not absolute**, correlation. It is submitted that the examples provided in the specification for nucleic acid sequences provide such reasonable correlation between the disclosure and the entire scope of a claim, including embodiments having therapeutically beneficial compound(s) other than nucleic acid sequences.

In view of the foregoing, it is the Applicant's position that the specification provides detailed, instruction-like disclosure, eliminating any need for undue experimentation.

Finally, the Applicant respectfully points out that it is only the necessity of undue experimentation that may make a specification non-enabling. Modest, reasonable quantity of experimentation is allowed, if it is routine or if the specification provides enough guidance. In re Wands, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). It has never been the rule that the

specification itself must necessarily describe how to use every possible variant of the claimed invention. Indeed, " the artisan's knowledge of the prior art and routine experimentation can often fill gaps, interpolate between embodiments, and perhaps even extrapolate beyond the disclosed embodiments." AK Steel Corp. v. Sollac, 344 F.3d 1234, 1244 (Fed. Cir. 2003).

Applying these principles to the facts of the present case, it is clear that since the specification provides enough guidance with respect to how to would require performing not more than common tasks routinely performed by competent artisans. There are also working examples. Accordingly, the Applicants respectfully submit that the specification properly enables claims 105 and 108-120. Reconsideration and withdrawal of the rejection are respectfully requested.

D. Rejection Under 35 U.S.C. § 103(a)

Claims 119 and 120 have been also rejected under 35 U.S.C. § 103(a) as allegedly being obvious in view of Unger (WO 94/28780) (page 18, lines 15-16 of the Office Action). The Applicants respectfully presume that the rejection applies to claim 119 and 120 (the Office action states "claims 19 and 20"). This rejection is respectfully traversed.

It is well establish that to properly state a *prima facie* case of obviousness, the Examiner must demonstrate that:

(a) there is some suggestion or motivation to modify the reference(s) as proposed by the Examiner;

(b) there is a reasonable expectation of success as a result of the modification; and

(c) so modified reference(s) teach or suggest all of the limitations of the claim at issue.

The Applicants respectfully submit that the above criteria have not been met. More specifically, claim 119 requires that the energy flux (i.e., wattage per 1 cm^2 of the surface) "200-500 milliwatts per cm^2" be used. Unger is completely silent with respect to the energy levels to

be used. All that is described by Unger is that the "higher energy ultrasound such as commonly employed in therapeutic ultrasound equipment is preferred" (see, page 56, lines 16-19) but does not describe the level of the energy flux to be used. In fact, it is submitted that Unger provides no suggestion or motivation to the energy flux of 200-500 mW per cm^2.

The Examiner has stated that the choice of energy flux in the instant claim 119 is merely "an optimum range." The Examiner has not provided any other explanation or justification why one skilled in the art will be motivated to modify Unger to arrive to what is claimed in claim 119, i.e., to claim the flux of 200-500 mW per cm^2. It is respectfully submitted that the rationale provided by the Examiner is insufficient to establish motivation. More is required, e.g., showing that the proposed modification is desirable.

It is well established that in making rejections over the prior art, the Patent Office "may not, because it may doubt that the invention is patentable, resort to speculation, unfounded assumptions or hindsight reconstruction to supply deficiencies in its factual basis." In re Warner, 379 F.2d 1011, 1017, 154 USPQ 173, 178 (CCPA 1967), cert. denied, 389 U.S. 1057, 19 L. Ed. 2d 857, 88 S. Ct. 811 (1968). It is submitted that the fact that the Examiner's has not provided a reasoned factual statement explaining the desirability of modifying Unger amounts to making such "unfounded assumptions or hindsight reconstruction."

Accordingly, the Applicants respectfully submit that the teachings of Unger cannot be properly modified due to lack of motivation to do so. In view of the foregoing, it is submitted that claim 119 is non-obvious and patentably distinguishable over Unger. Claim 120 depends on claim 119 and is considered patenatable for at least the same reason. Withdrawal of the rejection and reconsideration are respectfully requested.

E. Objections

The Examiner has objected to claim 117, due to a minor informality (page 3, lines 4-6 of the Office Action). Claim 117 have been amended and it is submitted that the objection no longer applies. Withdrawal of the objection and reconsideration are respectfully requested.

CONCLUSION

In view of the above amendments and remarks, reconsideration and favorable action on all claims are respectfully requested. In the event any matters remain to be resolved, the Examiner is requested to contact the undersigned at the telephone number given below so that a prompt disposition of this application can be achieved.

No fees are believed due in connection with the filing of this Response. However, the Commissioner is hereby authorized to charge any additional fees associated with the filing submitted herewith, or credit any overpayment, to Deposit Account No. 07-1896 referencing the above-identified attorney docket number. A duplicate copy of the Transmittal Letter is attached.

Date: July 27, 2006

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